## REMARKS

Claims 21, 23-29, and 31- 37 are pending in this application. Claims 1-20, 22, and 30 have been canceled. Claims 23, 28, 32, and 35 have been amended to correct typographical errors.

## REJECTIONS UNDER 35 U.S.C. § 102(a)

The Examiner has maintained the rejection of claims 21, 23-29, and 31 under 35 U.S.C. § 102(a) as allegedly anticipated by WO 00/29552. Applicants submit that WO 00/29552 is not prior art to the claimed invention and provide a Declaration Under 37 C.F.R. § 1.131 executed by both Dr. Manas Majumdar and Dr. Elisabeth Morris, the co-inventors of this application ("the Majumdar/Morris Declaration"). This Declaration demonstrates that the claimed invention was reduced to practice prior to May 25, 2000, the publication date of WO 00/29552.

Applicants incorporate by reference arguments made in support of this Declaration in the Amendment filed April 5, 2005 at pp. 6-9. Applicants have now established that they possessed "the whole invention claimed" prior to May 25, 2000. Thus, WO 00/29552 is not prior art and Applicants respectfully request that the rejection under 35 U.S.C. § 102(a) be withdrawn.

## REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 23, 24, 28, 29, 32, 33, 35, and 36 stand rejected as allegedly lacking enablement and written description under 35 U.S.C. § 112, first paragraph. The Examiner contends that the specification "does not reasonably provide enablement of

all bone or cartilage inducing factors" and that "Applicant has not provided any common characteristics by which the artisan could recognize individual members of this genus." (Office Action at page 3.) The Examiner further contends that the claims "contain subject matter not described in the specification in a way as to reasonably convey to one of skill in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention." (Office Action at pages 3-4.) Applicants traverse the rejections.

The Claimed Invention

The claims are directed to a method for inducing chondrogenesis by administering a composition comprising CD105+ cells. (See, specifically, claim 21.) The specification discloses that the compositions administered in the methods of the invention may *further* comprise bone and/or cartilage inducing factors to the CD105+ cells. (See, e.g., specification at page 6, lines 14-17.) The specification discloses that preferred bone and/or cartilage inducing factors include the transforming growth factor-beta (TGF-β) superfamily of proteins, bone morphogenetic proteins (BMPs), and growth differentiation factors (GDFs) (specification at page 6, line 22-24) and specifically identifies a large number of *known* bone and/or cartilage inducing factors (specification at page 6, line 19 to page 7, line 23).

Written Description

The Examiner rejected claims 23, 24, 28, 29, 32, 33, 35, and 36 as allegedly failing to comply with the written description requirement of 35 U.S.C. § 112, first paragraph.

The written description requirement serves to demonstrate that the applicant was in possession of the invention that is claimed. *In re Barker*, 559 F.2d 588, 592 n.4 (CCPA 1977) (the goal of the written description requirement is "to clearly convey the information that an applicant has invented the subject matter which is claimed"). Further, "[t]he descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific knowledge already in existence. *Capon v. Dudas*, 418 F.3d 1349, 76 USPQ2d 1078 (Fed. Cir. 2005) (holding that description of the structure of previously known claimed DNA material was not required in all cases where advances in the state of the art showed that one of skill in the art would readily understand the structure of the claimed DNA material from the methods described in the specification).

The Examiner alleges that the structural and functional features required for the desired bone and cartilage inducing activity are not provided, contending that members of the BMP family have different effects on the characteristic features of cartilage, so the identification of a molecule as a BMP is not sufficient to identify it as an agent that could be used in the instant methods. (Office Action at page 4.) Applicants disagree.

Applicants are not relying on the identification of a molecule as a BMP to describe the recited genus. Rather, Applicants are relying on the known bone and cartilage inducing activities of a number of members of the TGF-β superfamily and on the functional claim limitation of the term "bone and cartilage inducing factors." This description and the claim limitation clearly define the scope of the claims to the population of proteins that have bone and cartilage inducing activity. Moreover, Applicants specifically identify families of factors (TGF, BMP, GDF, etc) that are generally defined by common structural features (page 6, line 19 to page 7, line 23 of the specification). In addition, Applicants describe a significant number of individual species of the bone and/or cartilage inducing factors to support the recited genus.

As in *Capon*, where the structural features of known DNA segments did not need to be further described, additional descriptions of the structures of bone and cartilage inducing factors are not necessary because both their structures and their functions are well known in the art. The bone and/or cartilage inducing nature of these proteins are easily assessable by well-known methods, such as the Rosen-Modified Sampath Reddi rat bone formation assay, as disclosed in, e.g., U.S. Patent No. 5,013,649, which is incorporated by reference into the specification.

Furthermore, even if, as the Examiner asserts, BMP-12 and BMP-13 do not have the claimed bone and cartilage inducing activity, they are then not encompassed by the claims and thus do not need to be better described. The skilled artisan could readily determine whether a particular factor possesses bone and/or cartilage inducing activity.

If it does not, this same skilled artisan would recognize that it does not meet the limitation of the recited genus in the rejected claims.

Accordingly, Applicants submit that the application describes the species both structurally and functionally and that this description is sufficient to describe the genus of bone and cartilage inducing factors and request that this lack of written description rejection be withdrawn.

Enablement

To satisfy the enablement requirement, the specification must enable one skilled in the art to make and use the claimed invention without undue experimentation. *Atlas Powder Co. v. E.I. Du Pont de Nemours*, 750 F.3d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984) ("That some experimentation is necessary does not preclude enablement; the amount of experimentation, however, must not be unduly extensive.") The test considers more than the mere quantity of experimentation. *PPG Industries, Inc. v. Guardian Industries, Corp.*, 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1621 (Fed. Cir. 1996) ("[A] considerable amount of experimentation is permissible, if it is merely routine"); *see also*, *Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345, 56 USPQ2d 1332, 1337 (Fed. Cir. 2000) (holding that claims directed to a myriad of bacterial strains not yet known were enabled, where the identification and isolation techniques to discover the strains were well known).

Where, as here, the necessary methods to identify and produce the components for use in the claimed invention are well known and/or routine, the claims are enabled.

As noted above, the specification recites a number of well known bone and/or cartilage inducing factors that may be used in the claimed methods. The specification also recites and/or incorporates by reference numerous publications describing or defining the ability of these factors to induce bone and/or cartilage. Also well known in the art are techniques for assessing bone and/or cartilage inducing activity of a compound. Thus, not only have Applicants described a number of suitable bone and/or cartilage inducing factors that may be used in the methods of the invention, those of skill in the art can readily determine whether any particular compound functions as a bone and/or cartilage inducing factor. Nothing else is require for enablement.

The Examiner argues that Applicants have not provided any common characteristics by which the artisan could recognize individual members of the genus of "bone and/or cartilage inducing factors." (Office Action at page 3.) Applicants disagree. The functional requirement that the factor must induce bone and/or cartilage growth is the common characteristic of the recited genus.

The Examiner further argues that no common structures or other defining features have been provided. *Id.* Again, Applicants disagree. The specification identifies families of factors (TGF, BMP, GDF, etc) that are generally defined by common structural features.

The Examiner further contends that "[t]he art teaches that not even all members of the BMP family possess the required function," alleging that Valcourt et al., for

example, found that BMP-2 and BMP-4 induced both chondrocytic and osteoblastic markers in a chondrocyte cell line, whereas BMP-12 and BMP-13 had minimal effect.

First, Applicants disagree with the Examiner's characterization of the results shown in Valcourt. While BMP-12 and BMP-13 showed minimal effect in one assay, in the results shown in Figure 2, BMP-12 and BMP-13 induced an increase in chondrocyte cell growth similar to that of BMP-2 and BMP-4.

Furthermore, even if Valcourt did demonstrate that certain BMPs do not possess the claimed function, "it is not a function of the claims to specifically exclude . . . possible inoperative substances," and it is only when "the number of inoperative combinations becomes significant" that the claims may be held invalid. *Atlas Powder Co. v. E.I. Du Pont de Nemours*, 750 F.3d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984). The fact that BMP-12 and BMP-13 failed to upregulate cartilage markers in one cell line does not indicate that the claim scope, which encompasses many well-known bone and cartilage inducing factors, possesses a significant number of inoperative embodiments. And further, the ability to determine whether a given factor is operative or inoperative relies on well known and routine experimentation, and thus, does not present the skilled artisan with an undue burden.

In view of the arguments set forth above, Applicants submit that one of skill in the art can practice the methods of inducing chondrogenesis by administration of CD105+ cells alone, and can additionally select, without undue experimentation, bone and/or cartilage inducing factors to enhance the induction of chondrogenesis. If the bone or

cartilage inducing factor meets its functional limitation—the ability to induce bone and/or cartilage tissue—it is within the scope of the claims and will be enabled. Thus, Applicants respectfully request that the rejection of claims 23, 24, 28, 29, 32, 33, 35, and 36 as lacking enablement be withdrawn.

In view of the foregoing remarks, Applicants therefore request the entry of this Amendment, the Examiner's reconsideration and reexamination of the application, and the timely allowance of the pending claims. Please grant any extensions of time required to enter this response and charge any required fees to Deposit Account 06-0916.

Respectfully submitted,

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